

**WHAT IS CLAIMED IS:**

1. A peptide consisting of up to 51 amino acids comprising the sequence

**Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6,**

wherein:

the sequence is located at the N-terminal, C-terminal or at an interior position of the peptide;

Y1 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K, and R;

Y2 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K, and R;

Y3 is selected from the group consisting of I, V, L, A, S and T;

Y4 is selected from the group consisting of T, S, I, K, N, H, R, Q, E and D;

Y5 is selected from the group consisting of I, V, T, K, L, N, Q, D, E, R and H;

Y6 is selected from the group consisting of any amino acid except P, G and C; and,

each X independently is any amino acid.

2. A peptide consisting of up to 51 amino acids comprising the sequence

**Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7,**

wherein

Y1 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K, and R;

Y2 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K, and R;

Y3 is selected from the group consisting of I, V, L, A, S and T;

Y4 is selected from the group consisting of T, S, I, K, N, H, R, Q, E and D;

Y5 is selected from the group consisting of I, V, T, K, L, N, Q, D, E, R and H;

Y6 is selected from the group consisting of any amino acid except P, G and C;  
 Y7 is selected from the group consisting of I, L, V, N, Q, K, R, H, E and D;  
 and  
 each X independently is any amino acid.

3. A peptide consisting of up to 51 amino acids comprising the sequence

**Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8,**  
 wherein

Y1 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K, and R;

Y2 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K, and R;

Y3 is selected from the group consisting of I, V, L, A, S and T;

Y4 is selected from the group consisting of T, S, I, K, N, H, R, Q, E and D;

Y5 is selected from the group consisting of I, V, T, K, L, N, Q, D, E, R and H;

Y6 is selected from the group consisting of any amino acid except P, G and C;

Y7 is selected from the group consisting of I, L, V, N, Q, K, R, H, E and D;

Y8 is selected from the group consisting of Q, H, R, N, E, D, K and P; and  
 each X independently is any amino acid.

4. A peptide consisting of up to 51 amino acids comprising the sequence

**Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9,**

wherein

Y1 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K, and R;

Y2 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K, and R;

Y3 is selected from the group consisting of I, V, L, A, S and T;

Y4 is selected from the group consisting of T, S, I, K, N, H, R, Q, E and D;

Y5 is selected from the group consisting of I, V, T, K, L, N, Q, D, E, R and H;

Y6 is selected from the group consisting of any amino acid except P, G and C;

Y7 is selected from the group consisting of I, L, V, N, Q, K, R, H, E and D;

Y8 is selected from the group consisting of Q, H, R, N, E, D, K and P;

Y9 is selected from the group consisting of Q, H, N, E, D, K, R, L and P;

and

each X independently is any amino acid.

5. A peptide consisting of up to 51 amino acids comprising the sequence

**Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10,**

wherein

Y1 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K, and R;

Y2 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K, and R;

Y3 is selected from the group consisting of I, V, L, A, S and T;

Y4 is selected from the group consisting of T, S, I, K, N, H, R, Q, E and D;

Y5 is selected from the group consisting of I, V, T, K, L, N, Q, D, E, R and H;

Y6 is selected from the group consisting of any amino acid except P, G and C;

Y7 is selected from the group consisting of I, L, V, N, Q, K, R, H, E and D;

Y8 is selected from the group consisting of Q, H, R, N, E, D, K and P;

Y9 is selected from the group consisting of Q, H, N, E, D, K, R, L and P;  
Y10 is selected from the group consisting of Q, H, N, E, D, K and R; and  
each X independently is any amino acid.

6. A peptide of up to 51 amino acids comprising the sequence

**Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-  
Y9-Y10-X-X-Y11,**

wherein

Y1 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K,  
and R;

Y2 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K,  
and R;

Y3 is selected from the group consisting of I, V, L, A, S and T;

Y4 is selected from the group consisting of T, S, I, K, N, H, R, Q, E and D;

Y5 is selected from the group consisting of I, V, T, K, L, N, Q, D, E, R and  
H;

Y6 is selected from the group consisting of any amino acid except P, G and  
C;

Y7 is selected from the group consisting of I, L, V, N, Q, K, R, H, E and D;

Y8 is selected from the group consisting of Q, H, R, N, E, D, K and P;

Y9 is selected from the group consisting of Q, H, N, E, D, K, R, L and P;

Y10 is selected from the group consisting of Q, H, N, E, D, K and R;

Y11 is selected from the group consisting of N, S, T, V, A and D; and

each X independently is any amino acid.

7. A peptide of up to 51 amino acids comprising the sequence

**Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-  
Y9-Y10-X-X-Y11-Y12,**

wherein

Y1 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K,  
and R;

Y2 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K, and R;

Y3 is selected from the group consisting of I, V, L, A, S and T;

Y4 is selected from the group consisting of T, S, I, K, N, H, R, Q, E and D;

Y5 is selected from the group consisting of I, V, T, K, L, N, Q, D, E, R and H;

Y6 is selected from the group consisting of any amino acid except P, G and C;

Y7 is selected from the group consisting of I, L, V, N, Q, K, R, H, E and D;

Y8 is selected from the group consisting of Q, H, R, N, E, D, K and P;

Y9 is selected from the group consisting of Q, H, N, E, D, K, R, L and P;

Y10 is selected from the group consisting of Q, H, N, E, D, K and R;

Y11 is selected from the group consisting of N, S, T, V, A and D;

Y12 is selected from the group consisting of E, V, K, G, R, Q, D, N, H, T and S; and

each X independently is any amino acid.

8. A peptide of up to 51 amino acids comprising the sequence  
 Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-  
 Y9-Y10-X-X-Y11-Y12-X-X-Y13,

wherein

Y1 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K, and R;

Y2 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K, and R;

Y3 is selected from the group consisting of I, V, L, A, S and T;

Y4 is selected from the group consisting of T, S, I, K, N, H, R, Q, E and D;

Y5 is selected from the group consisting of I, V, T, K, L, N, Q, D, E, R and H;

Y6 is selected from the group consisting of any amino acid except P, G and C;

Y7 is selected from the group consisting of I, L, V, N, Q, K, R, H, E and D;  
 Y8 is selected from the group consisting of Q, H, R, N, E, D, K and P;  
 Y9 is selected from the group consisting of Q, H, N, E, D, K, R, L and P;  
 Y10 is selected from the group consisting of Q, H, N, E, D, K and R;  
 Y11 is selected from the group consisting of N, S, T, V, A and D;  
 Y12 is selected from the group consisting of E, V, K, G, R, Q, D, N, H, T  
 and S;  
 Y13 is selected from the group consisting of L, I, V, K and R; and  
 each X independently is any amino acid.

9. A peptide of up to 51 amino acids comprising the sequence  
**Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-  
 Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14,**

wherein

Y1 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K,  
 and R;

Y2 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K,  
 and R;

Y3 is selected from the group consisting of I, V, L, A, S and T;

Y4 is selected from the group consisting of T, S, I, K, N, H, R, Q, E and D;

Y5 is selected from the group consisting of I, V, T, K, L, N, Q, D, E, R and  
 H;

Y6 is selected from the group consisting of any amino acid except P, G and  
 C;

Y7 is selected from the group consisting of I, L, V, N, Q, K, R, H, E and D;

Y8 is selected from the group consisting of Q, H, R, N, E, D, K and P;

Y9 is selected from the group consisting of Q, H, N, E, D, K, R, L and P;

Y10 is selected from the group consisting of Q, H, N, E, D, K and R;

Y11 is selected from the group consisting of N, S, T, V, A and D;

Y12 is selected from the group consisting of E, V, K, G, R, Q, D, N, H, T  
 and S;

Y13 is selected from the group consisting of L, I, V, K and R;

Y14 is selected from the group consisting of L, S, M, Y, N, Q, E, D, K, and R; and

each X independently is any amino acid.

10. A peptide consisting of up to 51 amino acids comprising the sequence

Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14,

wherein:

Y2 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K, and R;

Y3 is selected from the group consisting of I, V, L, A, S and T;

Y4 is selected from the group consisting of T, S, I, K, N, H, R, Q, E and D;

Y5 is selected from the group consisting of I, V, T, K, L, N, Q, D, E, R and H;

Y6 is selected from the group consisting of any amino acid except P, G and C;

Y7 is selected from the group consisting of I, L, V, N, Q, K, R, H, E and D;

Y8 is selected from the group consisting of Q, H, R, N, E, D, K and P;

Y9 is selected from the group consisting of Q, H, N, E, D, K, R, L and P;

Y10 is selected from the group consisting of Q, H, N, E, D, K and R;

Y11 is selected from the group consisting of N, S, T, V, A and D;

Y12 is selected from the group consisting of E, V, K, G, R, Q, D, N, H, T and S;

Y13 is selected from the group consisting of L, I, V, K and R;

Y14 is selected from the group consisting of L, S, M, Y, N, Q, E, D, K, and R; and

each X independently is any amino acid.

11. A peptide of up to 51 amino acids comprising the sequence

**Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14,**

wherein:

Y3 is selected from the group consisting of I, V, L, A, S and T;

Y4 is selected from the group consisting of T, S, I, K, N, H, R, Q, E and D;

Y5 is selected from the group consisting of I, V, T, K, L, N, Q, D, E, R and H;

Y6 is selected from the group consisting of any amino acid except P, G and C;

Y7 is selected from the group consisting of I, L, V, N, Q, K, R, H, E and D;

Y8 is selected from the group consisting of Q, H, R, N, E, D, K and P;

Y9 is selected from the group consisting of Q, H, N, E, D, K, R, L and P;

Y10 is selected from the group consisting of Q, H, N, E, D, K and R;

Y11 is selected from the group consisting of N, S, T, V, A and D;

Y12 is selected from the group consisting of E, V, K, G, R, Q, D, N, H, T and S;

Y13 is selected from the group consisting of L, I, V, K and R;

Y14 is selected from the group consisting of L, S, M, Y, N, Q, E, D, K, and R; and

each X independently is any amino acid.

12. A peptide consisting of up to 51 amino acids comprising the sequence

**Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14,**

wherein:

Y4 is selected from the group consisting of T, S, I, K, N, H, R, Q, E and D;

Y5 is selected from the group consisting of I, V, T, K, L, N, Q, D, E, R and H;

Y6 is selected from the group consisting of any amino acid except P, G and C;



Y7 is selected from the group consisting of I, L, V, N, Q, K, R, H, E and D;

Y8 is selected from the group consisting of Q, H, R, N, E, D, K and P;

Y9 is selected from the group consisting of Q, H, N, E, D, K, R, L and P;

Y10 is selected from the group consisting of Q, H, N, E, D, K and R;

Y11 is selected from the group consisting of N, S, T, V, A and D;

Y12 is selected from the group consisting of E, V, K, G, R, Q, D, N, H, T  
and S;

Y13 is selected from the group consisting of L, I, V, K and R;

Y14 is selected from the group consisting of L, S, M, Y, N, Q, E, D, K, and  
R; and

each X independently is any amino acid.

13. A peptide consisting of up to 51 amino acids comprising the  
sequence

Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14,

wherein:

Y5 is selected from the group consisting of I, V, T, K, L, N, Q, D, E, R and  
H;

Y6 is selected from the group consisting of any amino acid except P, G and  
C;

Y7 is selected from the group consisting of I, L, V, N, Q, K, R, H, E and D;

Y8 is selected from the group consisting of Q, H, R, N, E, D, K and P;

Y9 is selected from the group consisting of Q, H, N, E, D, K, R, L and P;

Y10 is selected from the group consisting of Q, H, N, E, D, K and R;

Y11 is selected from the group consisting of N, S, T, V, A and D;

Y12 is selected from the group consisting of E, V, K, G, R, Q, D, N, H, T  
and S;

Y13 is selected from the group consisting of L, I, V, K and R;

Y14 is selected from the group consisting of L, S, M, Y, N, Q, E, D, K, and  
R; and

each X independently is any amino acid.

14. A peptide consisting of up to 51 amino acids comprising the sequence

**Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14,**

wherein:

Y6 is selected from the group consisting of any amino acid except P, G and C;

Y7 is selected from the group consisting of I, L, V, N, Q, K, R, H, E and D;

Y8 is selected from the group consisting of Q, H, R, N, E, D, K and P;

Y9 is selected from the group consisting of Q, H, N, E, D, K, R, L and P;

Y10 is selected from the group consisting of Q, H, N, E, D, K and R;

Y11 is selected from the group consisting of N, S, T, V, A and D;

Y12 is selected from the group consisting of E, V, K, G, R, Q, D, N, H, T and S;

Y13 is selected from the group consisting of L, I, V, K and R;

Y14 is selected from the group consisting of L, S, M, Y, N, Q, E, D, K, and R; and

each X independently is any amino acid.

15. A peptide consisting of up to 51 amino acids comprising the sequence

**W-X-X-W-X-X-X-I-X-X-X-T-X-X-I-X-X-L-I-X-X-X-Q-X-Q-Q-X-X-N,**

wherein:

each X independently is any amino acid.

16. A peptide consisting of up to 51 amino acids comprising the sequence

**W-X1-X2-W-X3-X4-X5-I-X6-X7-X8-T-X9-X10-I-X11-X12-L-I-X13-X14-X15-Q-X16-Q-Q-X17-X18-N-X19-X20-X21-X22-X23,**

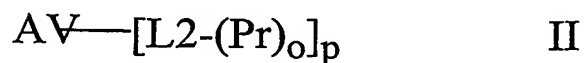
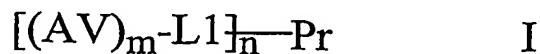
wherein:

X1 is selected from the group consisting of M, L, I, Q, T, R and K;

- X2 is either E, D, Q and K;  
X3 is selected from the group consisting of E, D and K;  
X4 is selected from the group consisting of K, R, E, Q, N and T;  
X5 is selected from the group consisting of E, L, R, K and Q;  
X6 is selected from the group consisting of N, D, S, E, Q, K, R, H, T, I and G;  
X7 is selected from the group consisting of N, Q, D, E, K, S, T and Y;  
X8 is selected from the group consisting of Y, F, H, I, V and S;  
X9 is selected from the group consisting of G, K, R, H, D, E, S, T, N and Q;  
X10 is selected from the group consisting of K, H, E, Q, T, V, I, L, M, A, Y, F, and P;  
X11 is selected from the group consisting of H, K, E, Y and F;  
X12 is selected from the group consisting of T, S, Q, N, E, D, R, K, H, W, G, A, and M;  
X13 is selected from the group consisting of D, E, Q, T, K, R, A, V and G;  
X14 is selected from the group consisting of D, E, K, H, Q, N, S, I, L, V, A and G;  
X15 is selected from the group consisting of S, A and (P);  
X16 is selected from the group consisting of N, K, S, T, D, E, Y, I and V;  
X17 is selected from the group consisting of E, D, N, K, G, and V;  
X18 is selected from the group consisting of K, R, H, D, E, N, Q, T, M, I, and Y;  
X19 is selected from the group consisting of E, V, Q, M, L, J, and G;  
X20 is selected from the group consisting of Q, N, E, K, R, H, L, and F;  
X21 is selected from the group consisting of E, D, N, S, K, A, and G;  
X22 is selected from the group consisting of L, I, and Y; and  
X23 is selected from the group consisting of I, L, M, Q, S, and Y.

17. The peptide of claim 16, wherein said peptide comprises a sequence selected from the group consisting of the sequences shown in Figure 1.

18. An isolated complex of the Formula I or Formula II:



wherein:

m is an integer from 1-5;

n is an integer from 1-100;

o is an integer from 1-5;

p is an integer from 1-100;

AV is an antiviral compound;

L1 and L2 are polyvalent linkers covalently linking AV to Pr, or where L1 and L2 are absent;

Pr is a protein; and

wherein the complex possesses antiviral activity in vivo.

19. The complex of Claim 18, wherein the antiviral compound is a peptide.
20. The complex of Claim 19 wherein the peptide has a mass of less than about 100 kDA.
21. The complex of Claim 19, wherein the peptide has a mass of less than about 30 kDA.
22. The complex of Claim 19, wherein the peptide has a mass of less than about 10 kDA.
23. The complex of Claim 19 wherein the peptide is a peptidomimetic.

24. The complex of Claim 19 wherein the peptide consists of up to 51 amino acids comprising a sequence selected from the group consisting of:

Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6;

Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7;

Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8;

Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9;

Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10;

Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11;

Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12;

Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13;

Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14;

Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14;

Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14;

Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14;

Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14;

Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14;

W-X-X-W-X-X-X-I-X-X-X-T-X-X-I-X-X-L-I-X-X-X-Q-X-Q-Q-X-X-N;

W-X1-X2-W-X3-X4-X5-I-X6-X7-X8-T-X9-X10-I-X11-X12-L-I-X13-X14-X15-Q-X16-Q-Q-X17-X18-N-X19-X20-X21-X22-X23;

peptide DP178 (T-20); and

peptide T-1249;

wherein:

- X1 is selected from the group consisting of M, L, I, Q, T, R and K;  
X2 is either E, D, Q and K;  
X3 is selected from the group consisting of E, D and K;  
X4 is selected from the group consisting of K, R, E, Q, N and T;  
X5 is selected from the group consisting of E, L, R, K and Q;  
X6 is selected from the group consisting of N, D, S, E, Q, K, R, H, T, I and G;  
X7 is selected from the group consisting of N, Q, D, E, K, S, T and Y;  
X8 is selected from the group consisting of Y, F, H, I, V and S;  
X9 is selected from the group consisting of G, K, R, H, D, E, S, T, N and Q;  
X10 is selected from the group consisting of K, H, E, Q, T, V, I, L, M, A, Y, F, and P;  
X11 is selected from the group consisting of H, K, E, Y and F;  
X12 is selected from the group consisting of T, S, Q, N, E, D, R, K, H, W, G, A, and M;  
X13 is selected from the group consisting of D, E, Q, T, K, R, A, V and G;  
X14 is selected from the group consisting of D, E, K, H, Q, N, S, I, L, V, A and G;  
X15 is selected from the group consisting of S, A and (P);  
X16 is selected from the group consisting of N, K, S, T, D, E, Y, I and V;  
X17 is selected from the group consisting of E, D, N, K, G, and V;  
X18 is selected from the group consisting of K, R, H, D, E, N, Q, T, M, I, and Y;  
X19 is selected from the group consisting of E, V, Q, M, L, J, and G;  
X20 is selected from the group consisting of Q, N, E, K, R, H, L, and F;  
X21 is selected from the group consisting of E, D, N, S, K, A, and G;  
X22 is selected from the group consisting of L, I, and Y; and  
X23 is selected from the group consisting of I, L, M, Q, S, and Y.

25. The complex of Claim 24 wherein the protein is a blood component.

26. The complex of Claim 25, wherein the blood component is selected from the group consisting of red blood cells, immunoglobulins, IgM, IgG, serum albumin, transferrin, P90 and P38, ferritin, a steroid binding protein, thyroxin binding protein, and  $\alpha$ -2-macroglobulin.

27. The complex of Claim 25, wherein the blood component is human serum albumin and the linker is a peptide linker.

28. The complex of Claim 25, wherein the blood component is human serum albumin and the linker is a non-peptide linker.

29. The complex of Claim 27, wherein the complex is a fusion protein.

30. The complex of Claim 18, wherein the linker L1 or L2 is a non-labile linker that is stable toward hydrolytic cleavage in vivo.

31. The complex of Claim 18 wherein the linker L1 or L2 comprises at least two functional groups covalently linking AV to Pr.

32. The complex of Claim 18 wherein the linker L1 or L2 is hydrolytically stable in human serum for an extended period of time.

33. The complex of Claim 18 wherein the linker L1 or L2 is stable in human serum for half lives of 8 hours to 30 days.

34. The complex of Claim 18 wherein the linker L1 or L2 is a derivative of a compound selected from the group consisting of acyloxymethylketones, aziridines, diazomethyl ketones, epoxides, iodo-, bromo- or chloroacetamides,  $\alpha$ -haloesters,  $\alpha$ -haloketones, sulfoniums, chloroethylsulfides, O-alkylisoureas, alkyl halides, vinylsulfones, acrylamides, acrylates, vinylpyridines, organometallic

compounds, aryl disulfides, thiosulfonates, aldehydes, nitriles,  $\alpha$ -diketones,  $\alpha$ -ketoamides,  $\alpha$ -ketoesters, diaminoketones, semicarbazones, and dihydrazides.

35. The complex of Claim 18 wherein the linker L1 or L2 is a derivative of a compound selected from the group consisting of azidobenzoyl hydrazide, N-[4-(p-azidosalicylamino)butyl]-3'-(2'-pyridyldithio)propionamide, bis-sulfosuccinimidyl suberate, dimethyl adipimidate, disuccinimidyl tartrate, N- $\gamma$ -maleimidobutyryloxysuccinimide ester, N-hydroxy sulfosuccinimidyl-4-azidobenzoate, N-succinimidyl [4-azidophenyl]-1,3'-dithiopropionate, N-succinimidyl [4-iodoacetyl]aminobenzoate, glutaraldehyde, succinimidyl 4-[N-maleimidomethyl]cyclohexane-1-carboxylate, N-hydroxysulfosuccinimide, maleimide-benzoyl-succinimide,  $\gamma$ -maleimido-butyryloxy succinimide ester, maleimidopropionic acid, N-hydroxysuccinimide, isocyanate, thioester, thionocarboxylic acid ester, imino ester, carbodiimide, anhydride and carbonate ester.

36. The complex of Claim 25 wherein the protein is albumin.

37. The complex of Claim 36, wherein the albumin is HSA or recombinant HSA that is at least 10% pure on a dry matter basis.

38. The complex of Claim 36, wherein the linkage is to a Cys-34 of human albumin.

39. The complex of Claim 36, wherein the linkage is to a lysine of human albumin.

40. The complex of Claim 18, wherein m is 1, n is 1, and the protein is HSA or recombinant HSA.



41. The complex of Claim 18, wherein n is 1, the protein is HSA or recombinant HSA, and wherein the complex is further purified to a purity of at least 30%.

42. The complex of Claim 18, wherein m is 1, n is 2, and the protein is HSA or recombinant HSA.

43. The complex of Claim 18, wherein the complex is prepared by combining a stoichiometric ratio of  $(AV)_m$ -L1 with Pr, or a stoichiometric ratio of AV with  $L2-(Pr)_o$ .

44. The complex of Claim 18, wherein the complex is prepared by combining a mixture of Pr to  $(AV)_m$ -L1 in a ratio of at least about 1.3:1.

45. The complex of Claim 18 where L1 and L2 are absent, and wherein the complex is prepared by forming an activated intermediate of AV followed by the condensation of the activated AV intermediate with Pr.

46. The complex of Claim 45, wherein the activated intermediate of AV is prepared from a mixed anhydride or  $N,N'$ -carbonyldiimidazole reagent.

47. The complex of any one of Claims 43-46 wherein the complex is further purified to a purity of at least about 30%.

48. An anti-viral composition comprising a non-peptidic anti-viral compound covalently linked to a blood component.

49. A composition comprising the complex of Claim 18 and a physiologically acceptable carrier.

50. The composition of Claim 49 formulated with saline or formulated without saline.

51. The composition of Claim 50 formulated for parenteral administration.

52. The composition of Claim 51 selected from the group consisting of solutions, dry products for combining with a solvent prior to use, suspensions, emulsions, and liquid concentrates.

53. A method for inhibiting the activity of HIV gp41 and HIV in vivo, the method comprising:

administering to the bloodstream of a mammalian host an isolated conjugate complex of Claim 18, wherein the complex is formed by attaching an antiviral compound to a linker having at least one reactive functional group which reacts with the protein to form stable covalent bonds; and

wherein the isolated conjugate complex is administered in an amount to maintain an effective therapeutic effect in the bloodstream for an extended period of time as compared to a non-conjugated antiviral compound.

54. The method of Claim 53 wherein the complex is the complex of Claim 26.

55. The method of Claim 53 wherein the protein is HSA or recombinant HSA.

56. The method of Claim 53 wherein the linker comprising a reactive functional group is a compound selected from the group consisting of acyloxymethylketones, aziridines, diazomethyl ketones, epoxides, iodo-, bromo- or chloroacetamides,  $\alpha$ -haloesters,  $\alpha$ -haloketones, sulfoniums, chloroethylsulfides, O-alkylisoureas, alkyl halides, vinylsulfones, acrylamides, acrylates, vinylpyridines,

organometallic compounds, aryldisulfides, thiosulfonates, aldehydes, nitriles,  $\alpha$ -diketones,  $\alpha$ -ketoamides,  $\alpha$ -ketoesters, diaminoketones, semicarbazones, and dihydrazides.

57. A method for eliciting antiviral activity in vivo, said method comprising:

administering into the bloodstream of a mammalian host the complex of Claim 18 in an amount sufficient to provide an effective amount for antiviral activity;

whereby said complex is maintained in the bloodstream over an extended period of time as compared to the lifetime of unbound antiviral compound.

58. A method for eliciting antiviral activity in a host, said method comprising:

a) preparing a compound AV-L1 or AV-L2 wherein AV is a peptide antiviral compound with a mass of less than 60 kD and L1 or L2 is a linker covalently bound to AV;

b) treating the compound AV-L1 or AV-L2 with isolated protein ex vivo for a time sufficient for the compound AV-L1 or AV-L2 to covalently bond to the protein to form the protein complex of Claim 18, and

c) administering the treated protein complex to the host.

59. The method of Claim 58, wherein the protein is albumin.

60. The method of Claim 59, wherein the albumin is HSA or recombinant HSA.

61. The method of Claim 59, wherein the albumin is obtained from blood, purified and isolated from blood prior to treating the albumin with the compound AV-L1 or AV-L2.

62. The method of Claim 61, wherein the albumin is purified to a purity level of at least 10% on a dry matter basis.

63. The method of Claim 61, wherein the albumin is purified to a purity level of more than 95%.

64. A method for eliciting antiviral activity in a host, said method comprising:

a) preparing a compound AV-L1 or AV-L2 wherein AV is an antiviral compound peptide with a mass of less than 60 kD and L1 or L2 is a linker covalently bound to AV;

b) treating the compound AV-L1 or AV-L2 with isolated one or more protein Pr ex vivo for a time sufficient for the compound AV-L1 or AV-L2 to covalently bond to one or more of the isolated proteins to form one or more modified protein complex of Claim 18; and

c) administering the modified protein or proteins to the host.

65. The method of Claim 64 wherein the protein is albumin.

66. The method of Claim 65 wherein the albumin is obtained from blood, purified and isolated from blood prior to treating with the compound AV-L1 or AV-L2.

67. The method of Claim 65 wherein the albumin is HSA or recombinant HSA.

68. A pharmaceutical composition comprising a therapeutically effective amount of a complex of Claim 18, or a physiologically acceptable salt thereof, and a pharmaceutically acceptable carrier, excipient, or diluent.

69. A process for inhibiting the action of the HIV virus which process comprises administering to a host in recognized need of such treatment an effective amount of a complex of Claim 18, or a pharmaceutically acceptable salt thereof.

70. A method of treating a subject suffering from a viral infection, comprising administering to said subject an effective amount of a composition of Claim 49.

71. A method of treating a subject suffering from a viral infection, comprising administering to said subject an effective amount of a composition of Claim 50.

72. A method of treating a subject suffering from a viral infection, comprising administering to said subject an effective amount of a composition of Claim 51.

73. A method of treating a subject suffering from a viral infection, comprising administering to said subject an effective amount of a composition of Claim 52.

74. The method of claim 70 wherein said subject is suffering from HIV infection.

75. The method of claim 71 wherein said subject is suffering from HIV infection.

76. A method of prophylaxis in a patient suspected of being exposed to a viral infection, comprising administering to said subject an effective amount of a composition of Claim 49.

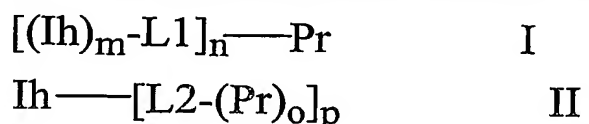
77. A method of prophylaxis in a patient suspected of being exposed to a viral infection, comprising administering to said subject an effective amount of a composition of Claim 50.

78. A method of prophylaxis in a patient suspected of being exposed to a viral infection, comprising administering to said subject an effective amount of a composition of Claim 51.

79. A method of prophylaxis in a patient suspected of being exposed to a viral infection, comprising administering to said subject an effective amount of a composition of Claim 52.

80. A method of prophylaxis in a patient suspected of being exposed to a viral infection, comprising administering to said subject an effective amount of a composition of Claim 53.

81. An isolated complex of the Formula I or Formula II:



wherein: m is an integer from 1-5; n is an integer from 1-100; o is an integer from 1-5; p is an integer from 1-100; Ih is a renin inhibitor; L1 and L2 are polyvalent linkers covalently linking Ih to Pr, or where L1 and L2 are absent; Pr is a protein; and wherein the complex possesses renin inhibitory activity in vivo.

82. The complex of Claim 81, wherein the renin inhibitor is a peptide.

83. The complex of Claim 82 wherein the peptide has a mass of less than about 60 kDA.

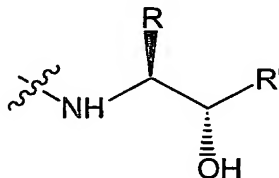
84. The complex of Claim 82, wherein the peptide has a mass of less than about 10 kDA.

85. The complex of Claim 82, wherein the peptide has a mass of less than about 1000 DA.

86. The complex of any of Claims 82-85 where the peptide is a peptidomimetic.

87. The complex of Claim 66, where the peptidomimetic is a transition state mimetic at the C-terminus.

88. The complex of Claim 87 wherein the transition state mimetic is a compound of the formula:

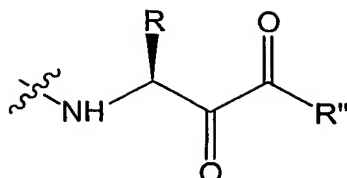


wherein:

R is selected from the group consisting of (C<sub>1-10</sub>)alkyl, (C<sub>6-12</sub>)cycloalkyl, carbonyl(C<sub>1-10</sub>)alkyl, sulfonyl(C<sub>1-3</sub>)alkyl, sulfinyl(C<sub>1-3</sub>)alkyl, (C<sub>2-12</sub>)alkenyl, (C<sub>2-12</sub>)alkynyl, aryl, aryl(C<sub>1-10</sub>)alkyl, heteroaryl, heteroaryl(C<sub>1-10</sub>)alkyl, each substituted or unsubstituted; and

R' is selected from the group consisting of (C<sub>1-10</sub>)alkyl, (C<sub>6-12</sub>)cycloalkyl, carbonyl(C<sub>1-10</sub>)alkyl, (C<sub>1-10</sub>)alkoxycarbonyl, (C<sub>1-10</sub>)alkylaminocarbonyl, sulfonyl(C<sub>1-3</sub>)alkyl, sulfinyl(C<sub>1-3</sub>)alkyl, (C<sub>2-12</sub>)alkenyl, (C<sub>2-12</sub>)alkynyl, aryl, aryl(C<sub>1-10</sub>)alkyl, heteroaryl, heteroaryl(C<sub>1-10</sub>)alkyl, alkylsulfonyl(C<sub>1-10</sub>)alkyl, arylsulfonyl(C<sub>1-10</sub>)alkyl, heteroarylsulfonyl(C<sub>1-10</sub>)alkyl, (C<sub>1-10</sub>)alkylphosphonate and (C<sub>1-10</sub>)alkyl phosphonyl, each substituted or unsubstituted.

89. The complex of Claim 87 wherein the transition state mimetic is a compound of the formula:

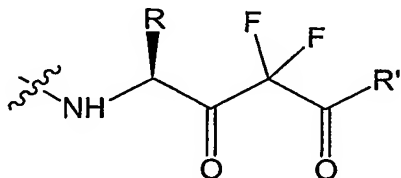


wherein:

R is selected from the group consisting of (C<sub>1-10</sub>)alkyl, (C<sub>6-12</sub>)cycloalkyl, carbonyl(C<sub>1-10</sub>)alkyl, sulfonyl(C<sub>1-3</sub>)alkyl, sulfinyl(C<sub>1-3</sub>)alkyl, (C<sub>2-12</sub>)alkenyl, (C<sub>2-12</sub>)alkynyl, aryl, aryl(C<sub>1-10</sub>)alkyl, heteroaryl, heteroaryl(C<sub>1-10</sub>)alkyl, each substituted or unsubstituted; and

R'' is selected from the group consisting of (C<sub>1-4</sub>)alkyl, (C<sub>6-12</sub>)cycloalkyl, heterocycloalkyl, bicycloalkyl, carbonyl (C<sub>1-10</sub>)alkyl, thiocarbonyl (C<sub>1-3</sub>)alkyl, sulfonyl (C<sub>1-3</sub>)alkyl, sulfinyl(C<sub>1-3</sub>)alkyl, amino, imino(C<sub>1-3</sub>)alkyl, (C<sub>1-10</sub>)alkoxy, aryloxy, heteroaryloxy, (C<sub>2-12</sub>)alkenyl, (C<sub>2-12</sub>)alkynyl, aryl, aryl(C<sub>1-10</sub>)alkyl, heteroaryl, heteroaryl(C<sub>1-10</sub>)alkyl, (C<sub>9-12</sub>)bicycloaryl, hetero(C<sub>8-12</sub>)bicycloaryl, aminosulfonyl, alkylsulfonyl, alkylsulfonyl(C<sub>1-10</sub>)alkyl, arylsulfonyl, arylsulfonyl(C<sub>1-10</sub>)alkyl, heteroarylsulfonyl, heteroarylsulfonyl(C<sub>1-10</sub>)alkyl, phosphonate, (C<sub>1-10</sub>)alkylphosphonyl, sulfonyl group and sulfinyl group, each substituted or unsubstituted.

90. The complex of Claim 87 wherein the transition state mimetic is a compound of the formula:



wherein:

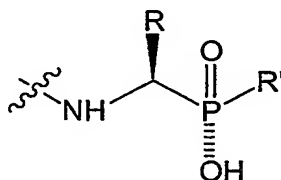
R is selected from the group consisting of (C<sub>1-10</sub>)alkyl, (C<sub>6-12</sub>)cycloalkyl, carbonyl(C<sub>1-10</sub>)alkyl, sulfonyl(C<sub>1-3</sub>)alkyl, sulfinyl(C<sub>1-3</sub>)alkyl, (C<sub>2-12</sub>)alkenyl, (C<sub>2-12</sub>)alkynyl, aryl, aryl(C<sub>1-10</sub>)alkyl, heteroaryl, heteroaryl(C<sub>1-10</sub>)alkyl, each substituted or unsubstituted; and

R'' is selected from the group consisting of (C<sub>1-4</sub>)alkyl, (C<sub>6-12</sub>)cycloalkyl, heterocycloalkyl, bicycloalkyl, carbonyl (C<sub>1-10</sub>)alkyl, thiocarbonyl (C<sub>1-3</sub>)alkyl,



sulfonyl (C<sub>1-3</sub>)alkyl, sulfinyl(C<sub>1-3</sub>)alkyl, amino, imino(C<sub>1-3</sub>)alkyl, (C<sub>1-10</sub>)alkoxy, aryloxy, heteroaryloxy, (C<sub>2-12</sub>)alkenyl, (C<sub>2-12</sub>)alkynyl, aryl, aryl(C<sub>1-10</sub>)alkyl, heteroaryl, heteroaryl(C<sub>1-10</sub>)alkyl, (C<sub>9-12</sub>)bicycloaryl, hetero(C<sub>8-12</sub>)bicycloaryl, aminosulfonyl, alkylsulfonyl, alkylsulfonyl(C<sub>1-10</sub>)alkyl, arylsulfonyl, arylsulfonyl(C<sub>1-10</sub>)alkyl, heteroarylsulfonyl, heteroarylsulfonyl(C<sub>1-10</sub>)alkyl, phosphonate, (C<sub>1-10</sub>)alkylphosphonyl, sulfonyl group and sulfinyl group, each substituted or unsubstituted.

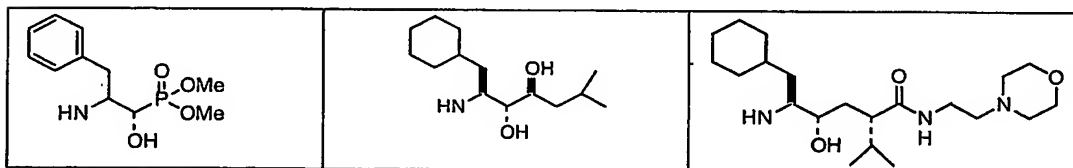
91. The complex of Claim 87 wherein the transition state mimetic is a compound of the formula:

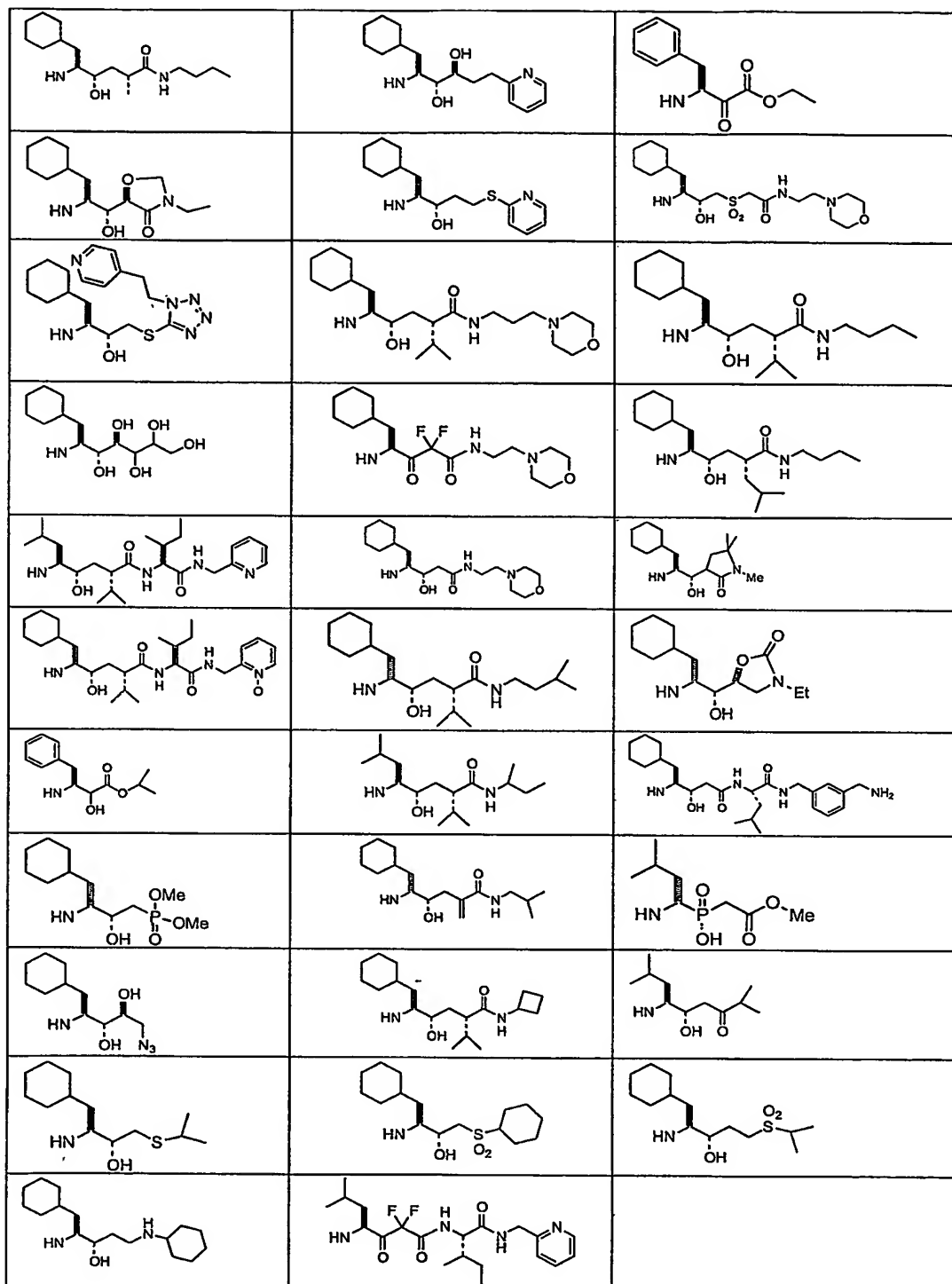


R is selected from the group consisting of (C<sub>1-10</sub>)alkyl, (C<sub>6-12</sub>)cycloalkyl, carbonyl(C<sub>1-10</sub>)alkyl, sulfonyl(C<sub>1-3</sub>)alkyl, sulfinyl(C<sub>1-3</sub>)alkyl, (C<sub>2-12</sub>)alkenyl, (C<sub>2-12</sub>)alkynyl, aryl, aryl(C<sub>1-10</sub>)alkyl, heteroaryl, heteroaryl(C<sub>1-10</sub>)alkyl, each substituted or unsubstituted; and

R' is selected from the group consisting of (C<sub>1-4</sub>)alkyl, (C<sub>6-12</sub>)cycloalkyl, heterocycloalkyl, bicycloalkyl, carbonyl (C<sub>1-10</sub>)alkyl, thiocarbonyl (C<sub>1-3</sub>)alkyl, sulfonyl (C<sub>1-3</sub>)alkyl, sulfinyl(C<sub>1-3</sub>)alkyl, amino, imino(C<sub>1-3</sub>)alkyl, (C<sub>1-10</sub>)alkoxy, aryloxy, heteroaryloxy, (C<sub>2-12</sub>)alkenyl, (C<sub>2-12</sub>)alkynyl, aryl, aryl(C<sub>1-10</sub>)alkyl, heteroaryl, heteroaryl(C<sub>1-10</sub>)alkyl, (C<sub>9-12</sub>)bicycloaryl, and hetero(C<sub>8-12</sub>)bicycloaryl, each substituted or unsubstituted.

92. The complex of Claim 87 wherein the transition state mimetic at the C-terminus is selected from the group consisting of





93. The complex of Claim 81 wherein Ih is a renin inhibitor peptide selected from the group consisting of Iva-Val-Val-Sta-Ala-Sta, Boc-Phe-His-Sta-Ile-

AMP, Boc-Phe-His-Sta-Ala-Sta-OMe, Boc-Phe-His-Sta-Leu-NHCH<sub>2</sub>Ph, Boc-Phe-His-ACHPA-Leu-AMB, Boc-Phe-His-Sta-Leu-AMB, Boc-Pro-Phe-His-Sta-Ile-AMP, Iva-Phe-Nle-Sta-Ala-Sta, Iva-His-Pro-Phe-His-Sta-Ala-Sta, Iva-His-Pro-Phe-His-Sta-Leu-Phe-NH<sub>2</sub>, Ac-His-Pro-Phe-Val-Sta-Leu-Phe-NH<sub>2</sub>, Ac-His-Pro-Phe-His-ACHPA-Leu-Phe-NH<sub>2</sub>, Ac-Trp-Pro-Phe-His-Sta-Ile-NH<sub>2</sub>, Ac-(HCO-Trp)-Pro-Phe-His-Sta-Ile-NH<sub>2</sub>, Pro-His-Pro-Phe-His-Sta-Ile-His-D-Lys, Pro-His-Pro-Phe-His-Sta-Ile-Phe-NH<sub>2</sub>, Z-Arg-Arg-Pro-Phe-His-Sta-Ile-His-Lys(Boc)-OMe, Pro-His-Pro-Phe-His-Phe-Phe-Val-Tyr-Lys, His-Pro-Phe-His-Leu-D-Leu-Val-Tyr-OH, Pro-His-Pro-Phe-His-Leu(CH<sub>2</sub>NH)Val-Ile-His-Lys (H-142), Boc-Phe-His-Cha-(CH<sub>2</sub>NH)Val-NH<sub>2</sub>(S)-Me(Bu), Pro-His-Pro-Phe-His-Leu-Phe-Val-Tyr-OH, Boc-His-Pro-Phe-His-Leu(CH(OH)CH<sub>2</sub>)Val-Ile-His-OH (H-261), and PEC-Phe-His-ACHPA-ILeNHC(CH<sub>2</sub>OH)<sub>2</sub>CH<sub>3</sub>.

94. The complex of Claim 81 wherein Ih is a renin inhibitor peptide selected from the group consisting of Iva-Val-Val-Sta-Ala-Sta, Boc-Phe-His-Sta-Ile-AMP, Boc-Phe-His-Sta-Ala-Sta-OMe, Boc-Phe-His-Sta-Leu-NHCH<sub>2</sub>Ph, Boc-Phe-His-ACHPA-Leu-AMB, Boc-Phe-His-Sta-Leu-AMB, Boc-Pro-Phe-His-Sta-Ile-AMP, Iva-Phe-Nle-Sta-Ala-Sta, Iva-His-Pro-Phe-His-Sta-Ala-Sta, Iva-His-Pro-Phe-His-Sta-Leu-Phe-NH<sub>2</sub>, Ac-His-Pro-Phe-Val-Sta-Leu-Phe-NH<sub>2</sub>, Ac-His-Pro-Phe-His-ACHPA-Leu-Phe-NH<sub>2</sub>, Ac-Trp-Pro-Phe-His-Sta-Ile-NH<sub>2</sub>, Ac-(HCO-Trp)-Pro-Phe-His-Sta-Ile-NH<sub>2</sub>, Pro-His-Pro-Phe-His-Sta-Ile-His-D-Lys, Pro-His-Pro-Phe-His-Sta-Ile-Phe-NH<sub>2</sub>, Z-Arg-Arg-Pro-Phe-His-Sta-Ile-His-Lys(Boc)-OMe, Pro-His-Pro-Phe-His-Phe-Phe-Val-Tyr-Lys, His-Pro-Phe-His-Leu-D-Leu-Val-Tyr-OH, Pro-His-Pro-Phe-His-Leu(CH<sub>2</sub>NH)Val-Ile-His-Lys (H-142), Boc-Phe-His-Cha-(CH<sub>2</sub>NH)Val-NH<sub>2</sub>(S)-Me(Bu), Pro-His-Pro-Phe-His-Leu-Phe-Val-Tyr-OH, Boc-His-Pro-Phe-His-Leu(CH(OH)CH<sub>2</sub>)Val-Ile-His-OH (H-261), and PEC-Phe-His-ACHPA-ILeNHC(CH<sub>2</sub>OH)<sub>2</sub>CH<sub>3</sub>, and Pr is albumin.

95. The complex of Claim 81 wherein the linker L1 or L2 comprises at least two functional groups covalently linking Ih to Pr.

96. The complex of Claim 81 wherein the linker L1 or L2 is hydrolytically stable in human serum for an extended period of time.

97. The complex of Claim 81 wherein the linker L1 or L2 is stable in human serum for half lives of 8 hours to 30 days.

98. The complex of Claim 81 wherein the linker L1 or L2 is a derivative of a compound selected from the group consisting of acyloxymethylketones, aziridines, diazomethyl ketones, epoxides, iodo-, bromo- or chloroacetamides,  $\alpha$ -haloesters,  $\alpha$ -haloketones, sulfoniums, chloroethylsulfides, O-alkylisoureas, alkyl halides, vinylsulfones, acrylamides, acrylates, vinylpyridines, organometallic compounds, aryldisulfides, thiosulfonates, aldehydes, nitriles,  $\alpha$ -diketones,  $\alpha$ -ketoamides,  $\alpha$ -ketoesters, diaminoketones, semicarbazones, and dihydrazides.

99. The complex of Claim 81 wherein the linker L1 or L2 is a derivative of a compound selected from the group consisting of azidobenzoyl hydrazide, N-[4-(p-azidosalicylamino)butyl]-3'-[2'-pyridyldithio]propionamide), bis-sulfosuccinimidyl suberate, dimethyl adipimide, disuccinimidyl tartrate, N-y-maleimidobutyryloxysuccinimide ester, N-hydroxy sulfosuccinimidyl-4-azidobenzoate, N-succinimidyl [4-azidophenyl]-1,3'-dithiopropionate, N-succinimidyl [4-iodoacetyl]aminobenzoate, glutaraldehyde, succinimidyl 4-[N-maleimidomethyl]cyclohexane-1-carboxylate, N-hydroxysulfosuccinimide, maleimide-benzoyl-succinimide,  $\gamma$ -maleimido-butyryloxy succinimide ester, maleimidopropionic acid, N-hydroxysuccinimide, isocyanate, thioester, thionocarboxylic acid ester, imino ester, carbodiimide, anhydride and carbonate ester.

100. The complex of Claim 81, wherein the protein is selected from the group consisting of red blood cells, and immunoglobulins, such as IgM and IgG, serum albumin, transferrin, p90 and p38.

101. The complex of Claim 100 wherein the protein is albumin.
102. The complex of Claim 101, wherein the albumin is HSA or recombinant HSA that is at least 10% pure on a dry matter basis.
103. The complex of Claim 101, wherein the linkage is to a Cys-34 of human albumin.
104. The complex of Claim 101, wherein the linkage is to a lysine of human albumin.
105. The complex of Claim 81, wherein m is 1, n is 1 or 2, and the protein is HSA or recombinant HSA.
106. The complex of Claim 81, wherein n is 1, the protein is HSA or recombinant HSA, and wherein the complex is further purified to a purity of at least 30%.
107. The complex of Claim 81, wherein m is 1, n is 2, and the protein is HSA or recombinant HSA.
108. The complex of Claim 81, wherein the complex is prepared by combining a stoichiometric ratio of  $(Ih)_m$ -L1 with Pr or a stoichiometric ratio of Ih with L2-(Pr)<sub>o</sub>.
109. The complex of Claim 81, wherein the complex is prepared by combining a mixture of Pr to  $(Ih)_m$ -L1 in a ratio of at least about 1.3:1.
110. The complex of Claim 81 where L1 and L2 are absent, and wherein the complex is prepared by forming an activated intermediate of Ih followed by the condensation of the activated Ih intermediate with Pr.

111. The complex of Claim 110, wherein the activated intermediate of Ih is prepared from a mixed anhydride or N,N'-carbonyldiimidazole reagent.

112. The complex of any of claims 108-11 wherein the complex is further purified to a purity of at least about 30%.

113. The complex of Claim 108, wherein the renin inhibitor is a peptidomimetic with a mass of less than about 1000 DA.

114. A composition comprising the complex of Claim 81 and a physiologically acceptable carrier.

115. The composition of Claim 114 formulated for parenteral administration.

116. The composition of Claim 115 selected from the group consisting of solutions, dry products for combining with a solvent prior to use, suspensions, emulsions, and liquid concentrates.

117. A method for inhibiting renin activity in vivo, said method comprising:

administering to the bloodstream of a mammalian host an isolated conjugate complex of Claim 81, wherein the complex is formed by attaching a renin inhibitor to a linker having at least one reactive functional group which reacts with the protein to form stable covalent bonds; and

wherein the isolated conjugate complex is administered in an amount to maintain an effective therapeutic effect in the bloodstream for an extended period of time as compared to a non-conjugated renin inhibitor.

118. The method of Claim 117 wherein the complex is the complex of Claim 100.

119. The method of Claim 117 wherein the protein is HSA or recombinant HSA.

120. The method of Claim 117 wherein the linker comprising a reactive functional group is a compound selected from the group consisting of acyloxymethylketones, aziridines, diazomethyl ketones, epoxides, iodo-, bromo- or chloroacetamides,  $\alpha$ -haloesters,  $\alpha$ -haloketones, sulfoniums, chloroethylsulfides, O-alkylisoureas, alkyl halides, vinylsulfones, acrylamides, acrylates, vinylpyridines, organometallic compounds, aryldisulfides, thiosulfonates, aldehydes, nitriles,  $\alpha$ -diketones,  $\alpha$ -ketoamides,  $\alpha$ -ketoesters, diaminoketones, semicarbazones, and dihydrazides.

121. A method for inhibiting renin activity in vivo, said method comprising:  
administering into the bloodstream of a mammalian host the complex of Claim 81 in an amount sufficient to provide an effective amount for renin inhibition;  
whereby said complex is maintained in the bloodstream over an extended period of time as compared to the lifetime of unbound renin inhibitor.

122. A method for inhibiting renin activity in a host, said method comprising:  
a) preparing a compound Ih-L1 or Ih-L2 wherein Ih is a renin inhibitor peptide with a mass of less than 60 kD and L1 or L2 is a linker covalently bound to Ih;  
b) treating the compound Ih-L1 or Ih-L2 with isolated protein ex vivo for a time sufficient for the compound Ih-L1 or Ih-L2 to covalently bond to the protein to form the protein complex of Claim 81, and  
c) administering the treated protein complex to the host.

123. The method of Claim 122, wherein the protein is albumin.

124. The method of Claim 123, wherein the albumin is HSA or recombinant HSA.

125. The method of Claim 123, wherein the albumin is obtained from blood, purified and isolated from blood prior to treating the albumin with the compound Ih-L1 or Ih-L2.

126. The method of Claim 125, wherein the albumin is purified to a purity level of at least 10% on a dry matter basis.

127. The method of Claim 125, wherein the albumin is purified to a purity level of more than 95%.

128. A method for inhibiting renin activity in a host, said method comprising:

a) preparing a compound Ih-L1 or Ih-L2 wherein Ih is a renin inhibitor peptide with a mass of less than 60 kD and L1 or L2 is a linker covalently bound to Ih;

b) treating the compound Ih-L1 or Ih-L2 with isolated one or more protein Pr ex vivo for a time sufficient for the compound Ih-L1 or Ih-L2 to covalently bond to one or more of the isolated proteins to form one or more modified protein complex of Claim 81; and

c) administering the modified protein or proteins to the host.

129. The method of Claim 128 wherein the protein is albumin.



130. The method of Claim 129 wherein the albumin is obtained from blood, purified and isolated from blood prior to treating with the compound Ih-L1 or Ih-L2.

131. The method of Claim 129 wherein the albumin is HSA or recombinant HSA.

132. A pharmaceutical composition comprising a therapeutically effective amount of a complex according to claim 81, or a physiologically acceptable salt thereof, and a pharmaceutically acceptable carrier, excipient, or diluent.

133. A method of reducing the blood pressure of a subject comprising administering to the subject a therapeutically effective amount of the composition according to claim 132.

134. The method according to claim 133, wherein said patient suffers from hypertension.

135. The method according to claim 134, wherein said patient suffers from mild, moderate or severe hypertension.

136. An isolated compound comprising a pharmacologically active moiety covalently conjugated to a macromolecular carrier,  
wherein the carrier is pharmacologically inert,  
wherein the linkage between said pharmacologically active moiety and said carrier is stable in vivo,  
wherein the intact compound substantially retains the pharmacological activity of said pharmacologically active moiety,  
and wherein the active half-life of said compound when administered to a mammal is at least about twice that of said pharmacologically active moiety.

137. The compound according to claim 136, wherein said macromolecular carrier is a protein.

138. The compound according to claim 136, wherein said macromolecular carrier is an albumin of homologous origin to said mammal.

139. The compound according to claim 138, wherein said albumin is a human serum albumin.

140. The compound according to claim 136, wherein said pharmacologically active moiety is conjugated to said carrier via a linker moiety.

141. The compound according to claim 136, wherein said pharmacologically active moiety is directly linked to said carrier.

142. The compound according to claim 136, wherein at least two pharmacologically active moiety molecules are conjugated to said carrier.

143. The compound according to claim 137, wherein the linkage to said carrier is via a lysine side chain on said carrier.

144. The compound according to claim 137, wherein the linkage to said carrier is via a cysteine side chain on said carrier.

145. The compound according to claim 136, wherein said carrier is HSA and the linkage is via C34 of the HSA.